Malaria Modeling and Surveillance

Verification and Validation Report

Part 1

Assessing Malaria Risks in Thailand Provinces
Using Meteorological and Environmental Parameters

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EXECUTIVE SUMMARY

Malaria has been with the human race since ancient times. Nowadays, most of the tropical and subtropical countries are endemic with malaria. There are approximately 300–500 million cases worldwide and at least 1 million deaths in any given year. The falciparum malaria, which has become drug resistant in most malarious areas, may become malignant and fatal without supportive care. The vivax and malariae malaria, although less virulent, may relapse and prolong morbidity. Before any effective vaccines become available, approximately 40% of the world's population is at risk.

Malaria transmission depends on the diverse factors that influence the vectors, parasites, human hosts, and the interactions among them. These factors may include, among others, meteorological and environmental condition, the innate and adapted immunity of the human hosts, public health system, housing standards, vector control, road construction, irrigation projects, population movements, and war-like conditions. The most apparent determinants are the meteorological and environmental factors, such as rainfall, temperature, humidity, and vegetation. When other factors remain more or less constant, the meteorological and environmental conditions can indeed be considered the driving factors. Remote sensing has been used in recent years for developing malaria early warning systems, particularly for Africa. For the Greater Mekong Subregion, an epicenter of multi-drug resistant malaria, there have been few studies to examine the dependency of malaria cases on these factors.

In an endemic area, the local adult population may acquire sufficient immunity after repeated infections. The disease could be deadly, however, to young children, pregnant women, those with depressed immunoresponse, and people new to the area. Because malaria is virtually nonexistent in the U.S., Americans traveling abroad and U.S. oversea forces are particularly vulnerable.

The goal of the NASA Malaria Modeling and Surveillance (MMS) project is to use NASA data, model outputs, and analytical and modeling expertise to enhance partners' decision support capabilities for malaria risk assessment and control. The technical objectives of the MMS project are: 1) identification of potential larval habitats for major malaria vector species; 2) estimation of current and prediction of future malaria risks; and 3) estimation of spatio-temporal transmission characteristics for cost-effective malaria control.

The Global Situational Awareness Tool (GSAT) is a system developed by the Air Force Special Operations Command (AFSOC) for assessing environmental and health issues of concerns for deployed U.S. forces. GSAT is a computerized set of linkable databases with an intelligent, user-friendly interface. It is designed as a knowledge or rule based system. The knowledge-based rules will be written by a group of experts to achieve outcomes as if human experts are performing similar analysis. The NASA and AFSOC teams first met in February, 2004 at the Tri-Service Entomological Conference in Jacksonville, Florida. It was thought that the two projects had compatible goals and that the GSAT might benefit from the MMS project's malaria risk assessments. A subsequent meeting was held at Stennis Space Center in August, 2004. An Evaluation Report was released in July 2005. The results from the MMS Project will be an essential element in deriving the rules for GSAT.

Neural network is a vital part of machine or artificial intelligence, which is a discipline to study machine's ability for learning and adaptation, and exhibition of intelligent behaviors. We have shown that neural network techniques are a useful approach for modeling the dependency of malaria cases on meteorological and environmental parameters.

Thailand has a long border—nearly 3,200 km over land—with Myanmar, Laos, Cambodia, and Malaysia as its neighboring countries. Attracted by economic opportunities and escaping from military conflicts, significant migrant and transient populations have come into Thailand. Due to the limited accessibility of health care, these populations expand the human reservoir for malaria transmission and escalate the endemicity among the native Thai population. The movement of migrant and transient populations around the border is an important contextual determinant that contributes to malaria transmission. In addition, it confounds the complexity for the prediction of malaria transmission intensity based on meteorological and environmental parameters.

We have used surface observed and satellite measured data to examine the dependency of malaria transmissions on meteorological and environmental factors. The malaria data are in provincial resolution. Malaria transmission is known to be spatially heterogeneous. In spite of the coarse resolution of the malaria data, we have uncovered a reasonable degree of dependency on the meteorological and environmental parameters. Based on the dependency, we can assess the current and future malaria risks.

With the simplest neural network architecture, the average training accuracy is approximately 73% among the three leading malarious provinces. More complex architectures will result in higher training accuracy. The average hindcasting accuracy is approximately 63% using the simplest (hence most robust) architecture. It should be noted that the training and hindcasting accuracy are not meant to be 100%, because the meteorological and environmental parameters only account for part of the factors that affect malaria transmissions. There is reason to believe that we can obtain a more precise meteorological and environmental association by using malaria data at higher resolution.

The risk assessments from the MMS project will allow the U.S. overseas forces better prepared in malaria prevention and in responding to malaria morbidity. In the Armed Forces, there are other Decision Support Systems similar to GSAT that provide risk assessments on infectious diseases. These systems exchange information with one another. At least two other systems use malaria risk assessments information. The beneficial returns of NASA data and results will be multiplied as the results from the MMS project are shared with other Decision Support Systems.

During peacetime or wartime, U.S. overseas forces work with the local public health organizations to reduce disease risks among the general populations. The outcome of the NASA MMS Project will therefore help reduce the morbidity and mortality among the local populations. The risk assessments will also facilitate more targeted insecticide and larvicide applications, and therefore reduce the potential damages to the environment and the risk of insecticide resistance.

1. INTRODUCTION

Malaria has been with the human race since ancient times. Nowadays, most of the tropical and subtropical countries are endemic with malaria. There are approximately 300–500 million cases worldwide and at least 1 million deaths in any given year. The falciparum malaria, which has become drug resistant in most malarious areas, may become malignant and fatal without supportive care. The vivax and malariae malaria, although less virulent, may relapse and prolong morbidity. The advances of biomedical research, and the completion of genomic mappings for *Plasmodium falciparum* (Gardner *et al.*, 2002) and *Anopheles gambiae* (Holt *et al.*, 2002) give hope for a reduced malaria burden in the future. Before any effective vaccines become available, however, approximately 40% of the world's population is at risk.

In an endemic area, the local adult population may acquire sufficient immunity after repeated infections. The disease could be deadly, however, to young children, pregnant women, those with depressed immunoresponse, and people new to the area. Because malaria is virtually nonexistent in the U.S., Americans traveling abroad and U.S. oversea forces are particularly vulnerable. For an immunologically naïve population arriving in an endemic region, preventive measures can be taken to minimize the impacts if malaria risks are known beforehand. Countermeasures can also be more effectively used to prevent outbreaks and contain malaria epidemics if such events can be forecasted. Since malaria transmissions are influenced by climatic and environmental factors, remote sensing can provide the essential information for malaria prevention and control.

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System engineering process is followed in enhancing GSAT with results from the MMS project. The Evaluation Phase resulted in the Evaluation Report that assesses the feasibility of enhancing the GSAT with results from the MMS project. The Verification and Validation (V&V) Phase examines the performance characteristics of the data, techniques, and models used in the MMS project and assessing their usefulness to GSAT. The Benchmarking Phase will measure the impact of the enhancement to GSAT.

Techniques developed for the first MMS objective is geographic-dependent, because they are driven by the ecology of the major mosquito species prevalent in that region. For example, *Anopheles sinensis* is responsible for the re-emerging of vivax malaria in Korea (Yeom et al., 2005). Its main larval habitats are irrigation and drainage ditches along rice fields. We have developed textural-contextual classification techniques to detect such potential larval habitats (Kiang et al, 2003).

This report addresses the V&V for the second objective – estimation of current and prediction of future malaria risks. We have used neural network to model meteorological and environmental dependency of malaria transmission in Thailand provinces. The development of the third technical objective on estimation of spatio-temporal transmission dynamic is on going. The V&V report for the third objective will be issued in FY07.

2. SUMMARY OF MMS-GSAT EVALUATION

The goals of AFSOC's GSAT and NASA's MMS Projects are clearly compatible. In the Evaluation Report, we concluded that the NASA data, results, and the output from MMS will be able to enhance GSAT's capability.

The NASA data and results to be provided to GSAT include: 1) the satellite derived meteorological and environmental parameters; 2) malaria risk maps for selected regions of the world that are jointly agreed upon by AFSOC and NASA teams; and 3) potential malaria vectors' larval habitats for selected areas. The NASA team will further develop its malaria modeling capabilities to assess malaria risks for regions of interest to AFSOC, while the AFSOC team will integrate malaria risks and NASA Earth-Sun science data into GSAT. The GSAT will also be tested by AFSOC 18th Flight Test Squadron and in real military exercises.

When GSAT is fielded, the Air Force will gain a computerized environmental and medical planning capability. The combined capabilities of the malaria assessments and GSAT will provide the U.S. Air Force, Department of Defense, and its partners with a decision support tool valuable to U.S. military and civilian sectors. Because U.S. oversea forces generally assist the local public health organizations in disease prevention and control, the enhanced GSAT will also benefit the local populations.

3. DESIGN AND IMPLEMENTATION

In this section, we will describe the data and methods that are used for modelling malaria risks. The meteorological and environmental parameters relevant to malaria transmissions are discussed first. In addition, epidemiological data are also needed in modelling. We will discuss how epidemiological data were obtained and their characteristics.

3.1 Environmental Determinants for Malaria Transmissions

The transmission of malaria is influenced by a myriad of factors. Environmental, climatic, social, and economic, public health, political, and warlike conditions have all been shown to contribute to malaria occurrence and outbreaks. Among these, the environmental conditions, especially rainfall, appears to be the most recognizable determinant. The intensity of malaria transmissions has long been associated with rainy seasons in human experience. The excessive rain or drought brought about by the climatic events like El Niño Southern Oscillation (ENSO) have also been shown to enhance the occurrence of malaria epidemics in the affected regions (Bouma & van der Kaay, 1996; Poveda *et al*., 2001; Githeko & Ndegwa, 2001; Gagnon *et al*., 2002; Kovats *et al*., 2003). Remote sensing is considered an important technology for predicting, preventing, and containing malaria epidemics (MARA/ARMA, 1998; WHO, 2001; WHO, 2004a; WHO, 2004b) because the environmental variables can be remotely sensed from satellites, and the likelihood of ENSO events may also be forecasted using satellite measured parameters. In recent years, researchers have used various methods and techniques that involves meteorological data or remotely sensed measurements for forecasting malaria epidemics, in particular for Africa (Thomson *et al.*, 1996; Hay *et al.*, 1998; Kleinschmidt *et al.*, 2000; Rogers *et al.*, 2002; Nalim *et al.*, 2002; Small *et al.*, 2003; Abeku *et al.*, 2004; Teklehaimanot *et al.*, 2004a; Teklehaimanot *et al.*, 2004b; Omumbo *et al.*, 2004; Thomson *et al.*, 2006). Some of the forecasting techniques may have already been used in operations (Grover-Kopec *et al.*, 2005). The advances in Geographic Information System (GIS) have also helped the integration of remote sensing measurements, epidemiological data, other information important to malaria transmission, and modeling results (Albert *et al.*, 2000).

Since rainfall provides vector breeding sites and prolongs vector life span by increasing humidity, precipitation or precipitation anomalies is the attribute most frequently used for predicting malaria epidemics. It has also been shown, however, that rainfall or the lack of it has a complex effect on malaria transmission for various parts of the world (Kovats *et al.*, 2003). For example, although moderate rainfall may promote malaria transmission, intense and prolonged rainfall may flush away larval habitats and thus reduce transmissions. Similarly, lack of rainfall does not always reduce larval populations. On the contrary, lack of rainfall may create new habitats, such as pools and puddles, in some regions and therefore increase larval population. In addition, droughts may be deleterious to predator populations or may cause human populations with no immunity to move to areas endemic with malaria (Kovats *et al.*, 2003). These factors may indirectly increase overall malaria transmissions. For regions where regular, yearly malaria infections contribute to partial immunity, a reduced transmission in certain years may increase the vulnerability in later years.

Another meteorological variable that is often used for predicting malaria transmission is temperature. Warmer temperature hastens larval and vector development and therefore increases the rate of vector production (Craig *et al.*, 1999). Temperature shortens the sporogonic cycle to allow vectors a longer period to transmit malaria. Warmer air also holds more moisture and therefore enhances mosquito survivorship.

The range of rainfall and temperature needed to maintain stable malaria transmission is called climate suitability (MARA/ARMA, 1998; Craig *et al.*, 1999; Small *et al.*, 2003; Omunbo *et al.*, 2004; Hay *et al.*, 2004). For example, in African regions where the *Anopheles gambiae* complex is the dominant species for transmitting falciparum malaria, climate suitability is associated with a temperature between 18º and 32º C and a rainfall exceeding 80 mm per month for at least 3 to 5 months (MARA/ARMA, 1998; Craig *et al.*, 1999).

Naturally, climate suitability depends on the ecology of the dominant malaria vector species. Therefore, it varies with geographic region (WHO & UNICEF, 2005). Climate suitability indicates how favorable the regional climate is for stable malaria transmission. How much this potential can be materialized into malaria endemicity, however, depends on other contextual determinants. Factors like socioeconomic conditions, public health infrastructures, herd immunity, irrigation and transportation projects, natural disasters, and military conflicts, have overriding effects on malaria transmission. When these contextual determinants are relatively unchanged, environmental determinants like rainfall and temperature are indeed the essential predictors for estimating the intensity of malaria transmission.

In the previous studies, rainfall surrogates were often used for modeling when no suitable remotely sensed or ground based measurements were available (Hay *et al.*, 1996; Thomson *et al.*, 1996; Hay *et al.*, 1998). The most frequently used surrogates include the Cold Cloud Duration (CCD) derived from the Meteosat measurements (Snijders, 1991) and the Normalized Difference Vegetation Index (NDVI) derived from the Advanced Very High Resolution Radiometer (AVHRR) measurements. The NDVI is not a measure of the precipitation at the time of the satellite overpass, but an increase in NDVI over nonirrigated area indicates the greening of vegetation and therefore implies that rainfall was recently received. The NDVI is also good for estimating the level of vegetation on the ground. It is therefore a useful indicator for differentiating between urban and rural areas. Direct, space-based rainfall measurements capabilities started with NASA's Tropical Rainfall Measuring Mission (TRMM) in 1999 (Kummerow *et al.*, 1998). TRMM is expected to last through 2009. The successor of the TRMM is the Global Precipitation Measurement (GPM) mission, an international collaboration involving a constellation of satellites (Flaming, 2005; Smith *et al.*, 2006).

Most malaria early warning capabilities developed to date are for Africa. It is generally agreed that rainfall excess is the main determinants for malaria epidemics in lowland and the warm, semi-arid and desert-fringe areas. For highland areas, temperature or temperature and rainfall together are the main predictors (Hay *et al.*, 2001; Thomson & Connor, 2001; Grover-Kopec *et al.*, 2005). The Greater Mekong Subregion (GMS), which consists of Thailand, Myanmar, Laos, Cambodia, Vietnam, and the Yunan Province of China, is an epicenter of multidrug resistant falciparum malaria (Kidson *et al.*, 1999). The Mekong Roll Back Malaria Program has identified remote sensing and GIS as important elements for malaria prevention and control in this region (Thimasarn, 2003). Remote sensing has been shown useful in Thailand for detecting potential larval habitats of malaria vectors and for estimating the associated malaria risks in the vicinity (Sithiprasasna *et al.*, 2005; Zollner *et al.*, 2006). Capabilities similar to those in Africa for malaria early warning are not yet available in the GMS.

An objective of the MMS project is to examine and model the meteorological and environmental dependency of malaria transmission in Thailand at provincial level. Because some satellite measurements were not yet available during the years in which the malaria epidemiological data were taken, meteorological data based on both ground observed and satellite sensed measurements are used. Therefore, a byproduct of this analysis is the feasibility of using meteorological and environmental data of mixed origins and resolution to estimate malaria endemicity at provincial resolution.

3.2 Epidemiological Data

All four human malaria species are present in Thailand. There are approximately equal number of *Plasmodium falciparum* and *P. vivax* malaria cases. Together, they account for approximately 99% of all the cases. *P. malariae* malaria cases are less than 1%, and *P. ovale* malaria is rare (Thai Ministry of Public Health, 2003). Through concerted efforts in surveillance and treatment, and prevention and control, malaria morbidity and mortality in Thailand has declined significantly in the last three decades. The current annual parasite incidence is less than 1 per 1000 population. Foreign workers and migrant, displaced populations from neighboring countries (Myanmar, Cambodia, Laos, and Malaysia) contribute significantly to malaria transmission in Thailand. Implementing positive health care policy for the non-Thai population in recent years has also helped lower malaria prevalence.

The monthly, provincial malaria data compiled by the Epidemiology Division, Department of Disease Control, Thai Ministry of Public Health (MOPH) are used in this study. These data are based on passive detections, which are essentially the confirmed malaria cases reported by hospitals and clinics. The data do not provide the information on parasite species. Annual (but not monthly) statistics with breakdowns into age groups and Thai or foreigner groups are also provided. Since it is not known whether the cases are new cases, recrudescence, or relapses, incidence rate cannot be directly calculated from the compiled data. In our analysis, we use the total monthly provincial malaria cases data that group parasite species and Thai or non-Thai populations together. Malaria data with higher spatial resolution (at district, village, and hamlet levels) and more details (parasite species, mixed infection, ages, and nationality) are archived at the Department of Disease Control.

Understandably, the data only include symptomatic cases. In Thailand, there may be a significant number of asymptomatic cases among repeatedly infected adults but the distribution may be geographically dependent (Coleman *et al.*, 2004; Pethleart *et al.*, 2004). In addition, there are an unknown number of symptomatic cases among the migrant and displaced populations who may not have sought or received treatments from public health organizations for a variety of reasons. The malaria cases used in the analyses therefore reflect the lower bound of the true prevalence.

Thailand requested Global Fund in 2002 to fight AIDS, tuberculosis, and malaria, and funding was started in 2004. For some reasons MOPH stopped releasing malaria epidemiological data in 2003. In addition, the quality of the data after 2000 has not been fully understood. For these reasons, we choose to use the data from 1994 to 2000.

3.3 Meteorological and Environmental Data

The malaria epidemiological data used for this analysis span from 1994 to 2000. For modeling and prediction, a variety of data sources will be needed to provide the meteorological and environmental data for this period and beyond.

<u>Temperature and Precipitation</u> Air temperature and precipitation data from 1994 to the end of 1999 are based on the Seasonal-to-Interannual Earth Science Information Partner (SIESIP) data set compiled by the Center for Climate Research of the University of Delaware. SIESIP is one of the Earth Science Information Partner (ESIP) projects funded by the National Aeronautics and Space Administration (NASA) to compile and develop customized Earth science data sets.

This data set was produced from the Global Historical Climatology Network (GHCN version 2) and Legates and Willmott's station records of monthly and annual mean air temperature and total precipitation. Using a spherical distance-weighting algorithm, station averages of monthly values were interpolated to a 0.5° x 0.5° latitude-longitude grid, with grid nodes centered on 0.25°. The number of nearby stations influencing grid node estimates was 20 on average. Both Digital Elevation Model-assisted interpolation and Climatologically Aided Interpolation were employed to estimate the monthly fields. This data set spans the time period from 1950–1999 (Vose *et al.*, 1992; Easterling *et al.*, 1996; Peterson & Vose, 1997).

From the beginning of 2000, we extracted the temperature data from the Moderate Resolution Imaging Spectroradiometer (MODIS) data set. MODIS has 2 bands at 250 m resolution, 5 bands at 500 m, and 29 bands at 1,000 m, with its spectral region ranging from visible to thermal wavelengths. MODIS is a key instrument on board the Terra Earth Observing System AM platform (EOS AM) and Aqua (EOS PM) satellites. Data from MODIS improve our understanding of global dynamics and processes occurring on the land, in the oceans, and in the lower atmosphere. A wide variety of geophysical parameters can be derived from MODIS measurements. To be precise, the temperature parameter in the MODIS product is land surface temperature instead of air temperature. However, the average monthly air temperature can be approximated by the average monthly land surface temperature, since these two parameters exhibit similar seasonal trend.

Also, from the beginning of 2000 we extracted the precipitation data from rainfall data sets measured by the instruments on board the Tropical Rainfall Measuring Mission (TRMM) spacecraft (Kummerow *et al.*, 1998). TRMM is a joint mission between NASA and the Japan Aerospace Exploration Agency designed to monitor and study tropical rainfall and to help our understanding of the water cycle in the climate system. Of the five instruments carried by TRMM, the Precipitation Radar and the TRMM Microwave Imager are most directly related to rain measurements. The TRMM precipitation data has a resolution of approximately 5 km at nadir.

When more than one data sources are used for a parameter, there may be intrinsic and valid differences due to the conditions under which the data were obtained. In these cases, a linear transformation was performed on the second data stream to match up the statistical properties of the first data stream.

Relative Humidity Relative humidity data were extracted from the National Centers for Environmental Prediction's (NCEP) Reanalysis Monthly Means and Other Derived Variables data set. The NCEP/National Center for Atmospheric Research (NCAR) Reanalysis Project uses a state-of-the-art analysis–forecast system to perform data assimilation using past data from 1948 to the present. A subset of this data was processed to create monthly means of a subset of the original data. These variables are instantaneous values at the reference time and are averages of instantaneous values at the four reference times—0, 6, 12, and 18 Z—over the averaging period. Spatial resolution of the data set is a 2.5° by 2.5° latitude/longitude global grid. Alternatively, if higher spatial resolution is needed, we can compute relative humidity from water vapor, which is one of the geophysical parameters available in the MODIS atmospheric profile product (MODIS atmosphere web site).

Vegetation Vegetation plays an important role in vector breeding, feeding, and resting sites. A number of vegetation indices have been used in remote sensing and Earth science disciplines. The most widely used index is the Normalized Difference Vegetation Index (NDVI) (Tucker, 1979). It is simply defined as the difference between the red and the near infrared bands normalized by twice the mean of these two bands. For green vegetation, the reflectance in the red band is low because of chlorophyll absorption, and the reflectance in the near infra-red band is high because of the spongy mesophyll leave structure. The more vigorous and denser the vegetation is, therefore, the higher the NDVI becomes.

NDVI has also been used as a surrogate for rainfall estimate. It is an effective measure for arid or semi-arid region. For tropical regions where ample rainfall is normally received, vegetation index may be a less sensitive measure for estimating rainfall. The mean vegetation index over a region does reflect the degree of urbanization or lack of vegetation. In this sense, NDVI in a grid cell is used as an indicator for the mean level of vegetation present in the cell.

Any satellite instrument with red and infrared bands can be used to compute NDVI. However, because of the difference in band definitions, spatial resolutions, and satellite passing time, NDVI computed from different sensors must first be calibrated before the NDVI from different sensors can be compared.

The NDVI data are processed and distributed by the NASA Goddard Space Flight Center's Distributed Active Archive Center (DAAC). These data are 8 km resolution monthly NDVI maximum value composite images (DAAC interdisciplinary data and resources web site). The original data set was produced as part of the National Oceanic and Atmospheric Administration (NOAA)/NASA Pathfinder Advanced Very High Resolution Radiometer (AVHRR) Land Program. The data set spans July 1981 through December 2000, with the exception of September through December 1994.

We use the NDVI data for 2000 and beyond from the MODIS measurements (MODIS atmosphere web site).

A sample of the meteorological and environmental parameters used for modeling, including precipitation, temperature, relative humidity, and vegetation index, are shown in Figs. 1-4 for the four Thailand seasons. The four Thailand seasons, classified according to temperature and rainfall, are cool-dry (November, December, and January), hot-dry (February, March, and April), early rainy (May, June, and July), and late rainy (August, September, and October) seasons.

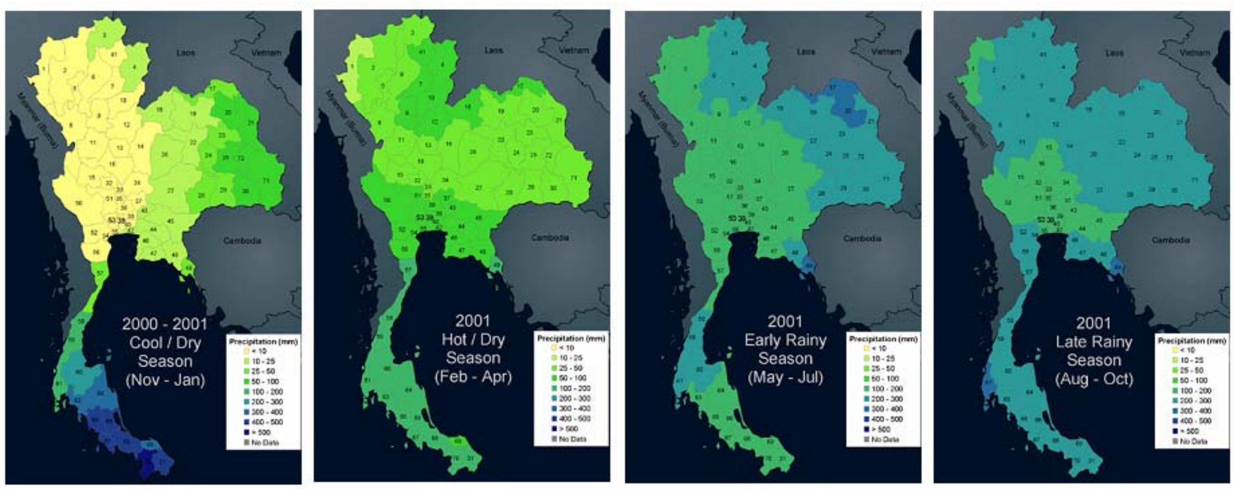

Figure 1. Precipitation for the four Thailand seasons (2000–2001).

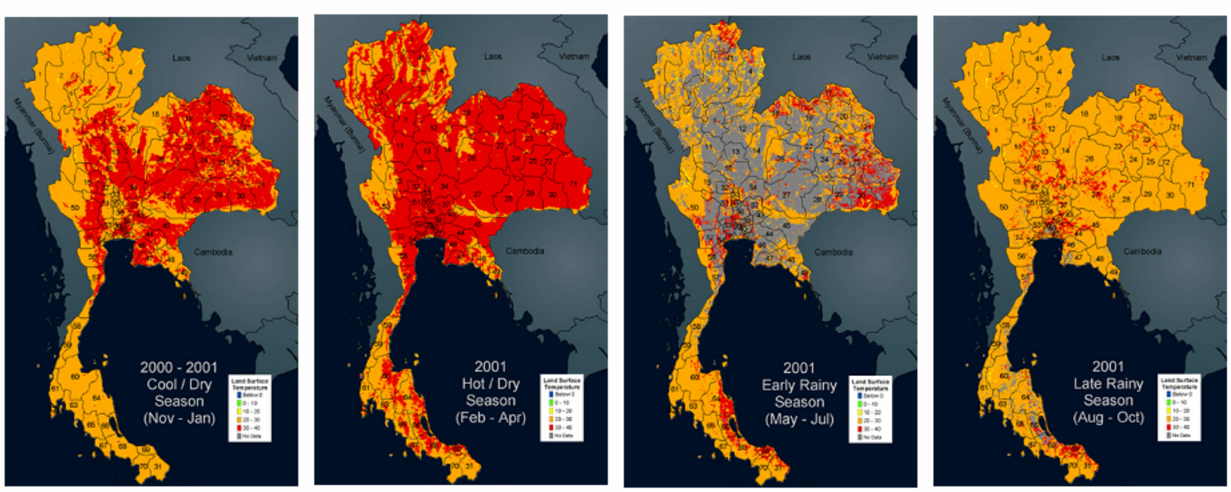

Figure 2. Surface air temperature for the four Thailand seasons (2000–2001).

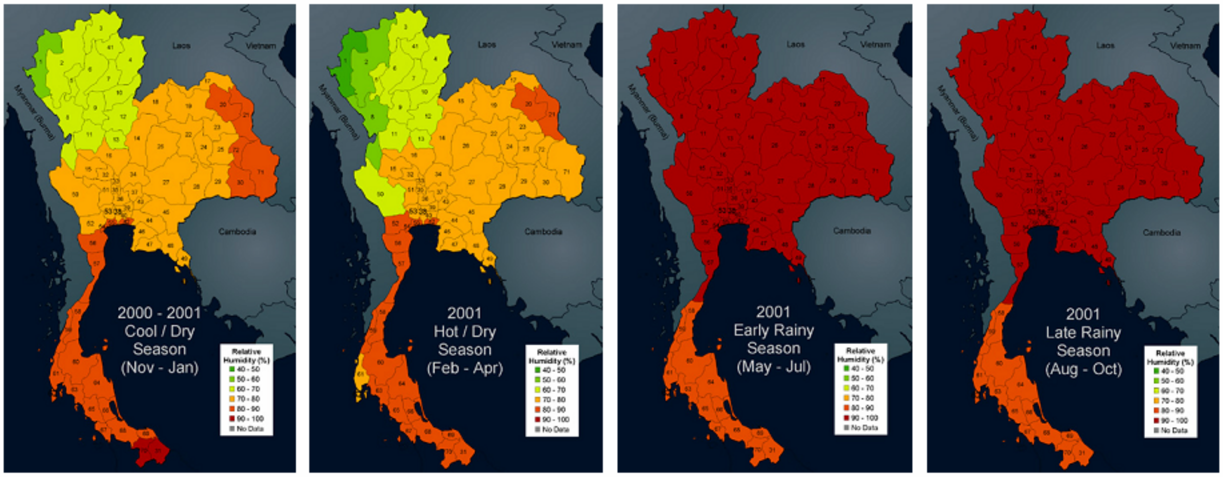

Figure 3. Relative humidity for the four Thailand seasons (2000–2001).

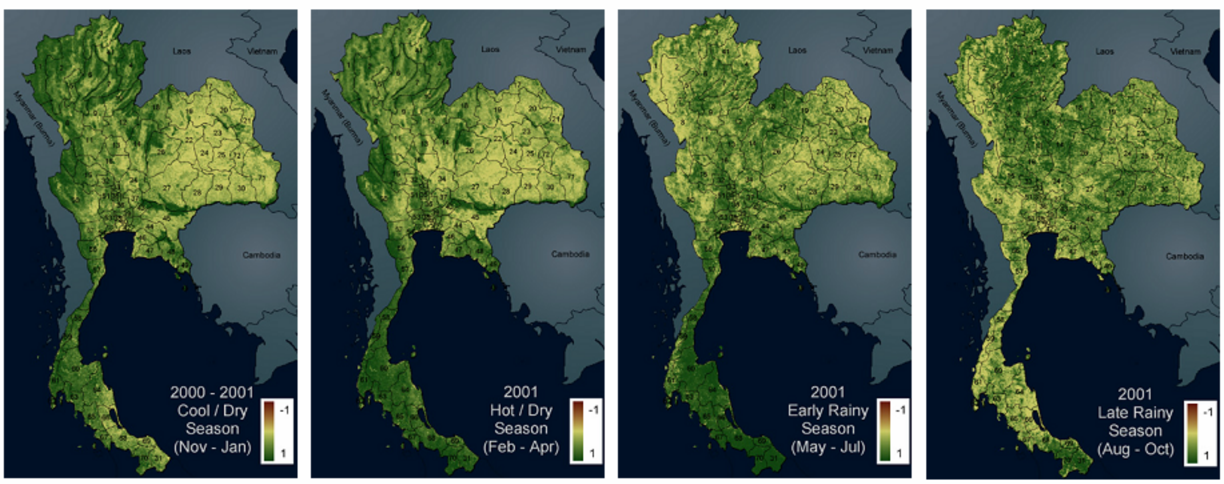

Figure 4. NDVI for the four Thailand seasons (2000–2001).

3.4 Modeling Malaria Risks

We use the neural network (NN) method to approximate the dependency of malaria cases on the meteorological and environmental variables. This method has been successfully used in many applications, including classification, regression, time series analysis, and handwritten character recognition (Nelson & Illingworth, 1990). In this approach, the probability density of the data is not assumed to follow any particular functional form. Rather, the characteristics of the probability density are determined entirely by the distribution in the data, hence, it is a data driven approach. This method is most suitable for problems that are too complex to be expressed in a closed, analytical form. For problems in which there are hidden, implicit variables, this approach is particularly suitable, as it is difficult to either specify the variables properly or sufficiently account for their effects mathematically.

This method is called neural network because it resembles how biological neurons function (Gardner, 1993). Nodes in a neural network are analogous to neurons. The connections between the nodes are analogous to synapses. The behavior of the activation function corresponds to the firing of a neuron. The weights of the connections can be trained to give the aggregate of neurons a specific functionality. A network may accommodate complicated geometries in multidimensional space by incorporating hidden layers. Without hidden layers, the neural network method will be equivalent to the generalized linear model.

To train our neural network model, we feed observed or measured parameters from the past into the network. The input parameters may consist of meteorological, environmental, and other variables and the output parameter is the corresponding malaria cases for that specific location and time. Once trained, the network will be able to estimate the cases at some other time period using the parameters corresponding to that time period.

The neural network used in this analysis is in the class of multi-layer perceptron (Rumelhart & McClelland, 1986; Haykin, 1994; Bishop, 1996). The general network architecture is composed of an input layer, one or more hidden layers, and an output layer. Each layer consists of a number of nodes. In this analysis, meteorological and environmental data are the main parameters fed into the input layer; and the malaria cases or other data indicating malaria prevalence are the parameters generated from the output layers. A hidden layer consists of one or more hidden nodes. The function of the hidden layers in a neural network is to map the data structure into a new representation that facilitates the optimization of the objective function. For example, if the objective function is to maximize classification accuracy, hidden layers will transform the input parameters into functions of the parameters to make the classes more readily separable. Without hidden layers, a neural network may only differentiate linearly separable classes. Because the complexity of the data structure and the objective function drive the construction of hidden layers, trial and error is the usual approach to determine the numbers of hidden layers and hidden nodes to be used. In fully interconnected networks, weight decay (Bishop, 1996) can be used to eliminate nodes and links that are insensitive to the optimization of the objective function.

In the hindcasting (or retrospective forecasting) mode, the model is used to estimate the historical cases. The model's estimation accuracy can then be determined by comparing the model output with the events that took place in the past. Moreover, future malaria cases can be predicted by using forecast parameters as input in the forecasting mode. Once a model is trained with past epidemiological data for a region, estimates on current malaria endemicity for that region can also be obtained by feeding current meteorological and environmental data into the trained model.

We developed the majority of the processing, modeling, and analysis software in IDL and C, including a neural network code in C. Commercial software used in this study includes ENVI/IDL 4.0, Matlab, NeuroSolution, and ArcView 9.

4. V&V METHODS AND RESULTS

For the remainder of this report, we denote the average surface temperature by T, the precipitation amount by P, the precipitation amount in the previous month by P_{-1}, the relative humidity by H, and vegetation index by V. The major malaria vector species in Thailand include *Anopheles dirus*, *An. minimus*, and *An. maculatus*. Increase in precipitation generally creates more larval habitats. This leads to an increase in mosquito population, and more intense transmissions.

Various neural network architectures were used in this analysis. The most suitable architecture may vary from province to province. For the ease of discussion, four configurations are reported in the following – networks with one hidden layer (HL) imbedded with one, two, or three hidden nodes (HN). The input variables include P, P_{-1}, T, H, V. Time, t, is also used as an input parameter to account for trends that are independent of meteorological and environmental variables. The trend can be linear or nonlinear. For example, this time factor may reflects the advances in malaria detection and treatment methods, improvement in public health support, establishment of more plantations, construction of transportation routes and irrigation projects, and changes in the influx of refugees and migrant populations. In general, the time factor helps to account for the effects of the changes in non-meteorological and non-environmental contextual parameters on malaria transmission during the time period under study. A typical network architecture is depicted in Fig. 5.

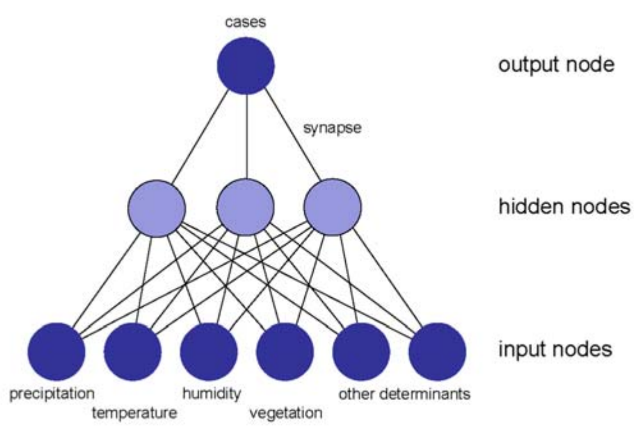

Figure 5. A typical neural network architecture.

To examine how well these configurations perform for the three most endemic provinces – Kanchanaburi, Mae Hong Son, and Tak, the malaria data from 1994 to 2000 are divided into 6 groups. Each group consists of 5 years of data for training and 1 year of data for testing. The average over the 6 groups of the root-mean-square error between the real cases and the fitted cases normalized by the real cases is used as an accuracy measure.

The network for each input data combination was trained using backward propagation (Haykin, 1994; Bishop, 1996) for a million epochs or until the training errors converged. An epoch is a complete round of training over all the input samples. Although the training might not have completely converged after a million epochs, the decrease in the value of the objective function and the changes in the network parameters at this point were negligibly small from one epoch to the next.

Table 1 shows the training and testing results from the neural network. Configuration 1 has the simplest architecture. For example, the average training accuracy is 75±9%, and testing accuracy is 67±10% for Kanchanaburi. Like in other classification techniques, the training accuracy is normally higher than the testing accuracy. This is due to the differences in statistical characteristics between the training and testing samples. In the context of the MMS project, it implies that malaria transmission in the training and testing samples may respond differently to changes in meteorological and environmental parameters, and that some other contextual determinants are not stationary. When the temperature parameter is removed from the input (in Configuration 2), the accuracy for Kanchanaburi is somewhat reduced to 74±9% and 62±12% respectively for training and testing. When another hidden node is included in Configuration 3, more complex geometries can be constructed to assure better classification. For example, the average training accuracy becomes 83±6% for Kanchanaburi. The testing accuracy, however, reduces to 57±16%. This indicates that the more complex geometry might have been constructed to accommodate the noise components in the training samples, and thus worsened the testing accuracy. When one more hidden node is included in Configuration 4, the training accuracy continues to increase. The testing accuracy continues to decrease and becomes erratic for Mae Hong Son. This indicates that the network is over trained. The changes of training errors vs. iterations for Configurations 1 & 4 are shown in Fig. 6.

Table 1. Training and testing accuracy in using neural networks with various architecture to assess malaria risks.

	Configuration 1 t, T, P, P_{-1}, H, V I HL 1 HN		Configuration 2 t, P, P_{-1}, H, V I HL 1 HN		Configuration 3 t, T, P, P_{-1}, H, V I HL 2 HN		Configuration 4 t, T, P, P_{-1}, H, V I HL 3 HN	
Province	training	testing	training	testing	training	testing	training	testing
Kanchanaburi	75±9%	67±10%	74±9%	62±12%	83±6%	57±16%	88±4%	58±17%
Mae Hong Son	71±10%	57±11%	69±11%	56±6%	77±8%	56±7%	84±6%	10±50%
Tak	72±10%	64±6%	70±11%	63±8%	78±8%	55±20%	84±6%	48±22%

Weight decay (Bishop, 1996) may reduce the effective number of synapses and nodes in a fully connected network. Therefore, it allows more complex architectures with a lower degree of freedom. How this may improve training and prediction accuracy is being studied. We will describe the result in a follow-on report if this technique is proved useful.

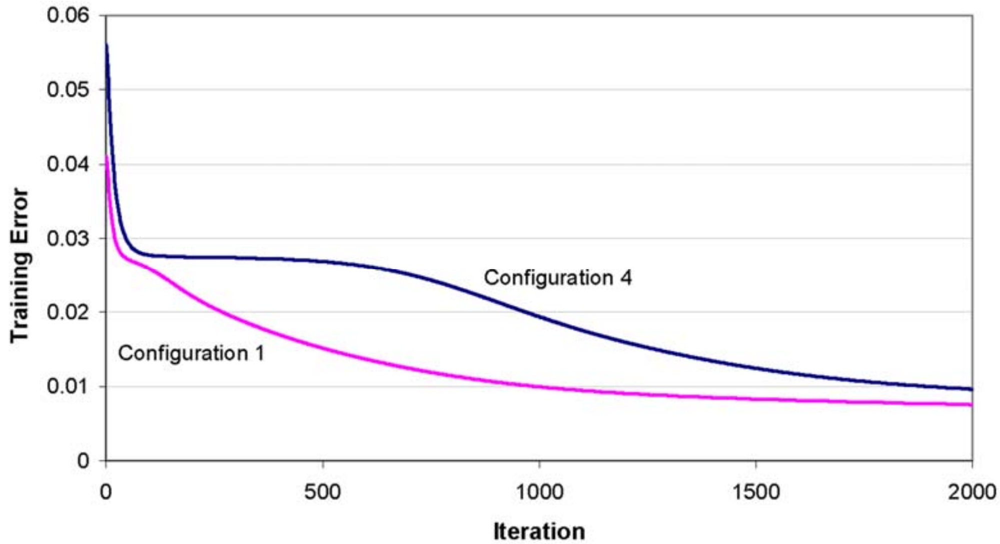

Figure 6. Training errors decrease as neural networks go through iterations to seek optimum parameters.

In the formulation described above, training accuracy is expressed as normalized root-mean-square error by comparing network output with malaria cases. Because of the intrinsic uncertainty in the reported malaria cases due to, for example, inaccurate microscopy reading, asymptomatic cases, and unreported cases in transient populations, accuracy measures may be defined less stringently in the following way. We divided the malaria cases into 20 bands – from zero to 1.5 times of the historical maximum. The classification will be considered correct as long as the fitted data falls into the correct band or one of the two adjacent bands. The upper limit of the highest band was set to infinity. We then apply the architecture used for Configuration 1 in Table 1 to the malaria data for the 19 provinces more endemic with malaria between 1994 and 2000. Aside from Kanchanaburi, Mae Hong Song, and Tak that were selected before, the other 16 provinces are, in alphabetical order, Chanthaburi, Chiang Mai, Chymphon, Krabi, Narathiwat, Phetchaburi, Prachinburi, Prachuap Khiri Khan, Ranong, Ratchaburi, Rayong, Suphan Buri, Surat Thani, Trat, Ubon Ratchathani, and Yala. The malaria endemicity in the other 57 provinces in Thailand is very low or none. The training accuracy results from these 19 provinces and the width of each band are shown in Table 2. When weighed by the populations, the average training accuracy of the 19 provinces is 73%.

In general, collection of reliable malaria epidemiological data, especially through active case detection, is a major undertaking for public health agencies. Compiling and maintaining the records from all levels of hospitals, clinics, mobile units, and volunteer outposts also need substantial resources. Among the developing countries that are endemic with malaria, there is a general scarcity of reliable malaria data. Taking Indonesia for example, the data gaps are so extensive that we need to develop new techniques to analyze the data we could obtain. Even when surveillance data are available, malaria data in some countries are sometimes withheld or manipulated to suit political purposes. The ability to estimate current malaria endemicity based on malaria data from the past is therefore very important.

Our risk assessment model, once trained, can be used to estimate current or future malaria endemicity by feeding the current or the forecasted meteorological parameters into the model. For example, although Thailand has stopped releasing malaria data, the current malaria endemicity can still be estimated using our model. Fig. 7 shows the estimated average malaria cases in July 2006 for the 19 most malarious provinces based on Thailand's climatology data from the past 3 years. Alternatively, the observed meteorological data can be used to estimate the current cases.

Table 2. Training accuracy for the 19 Thailand provinces most endemic with malaria using neural networks. Malaria cases are grouped into bands to account for the uncertainty in the reported malaria cases. Widths of the bands expressed in number of malaria cases are also shown.

Province	Training Accuracy	Band Width
Chanthaburi	0.55	180
Chiang Mai	0.57	84
Chymphon	0.70	140
Kanchanaburi	0.73	503
Krabi	0.76	59
Mae Hong Son	0.88	435
Narathiwat	0.81	83
Phetchaburi	0.74	92
Prachinburi	0.64	23
Prachuap Khiri Khan	0.95	287
Ranong	0.77	126
Ratchaburi	0.79	182
Rayong	0.61	35
Suphan Buri	0.61	27
Surat Thani	0.76	304
Tak	0.64	408
Trat	0.45	203
Ubon Ratchathani	0.52	91
Yala	0.86	112

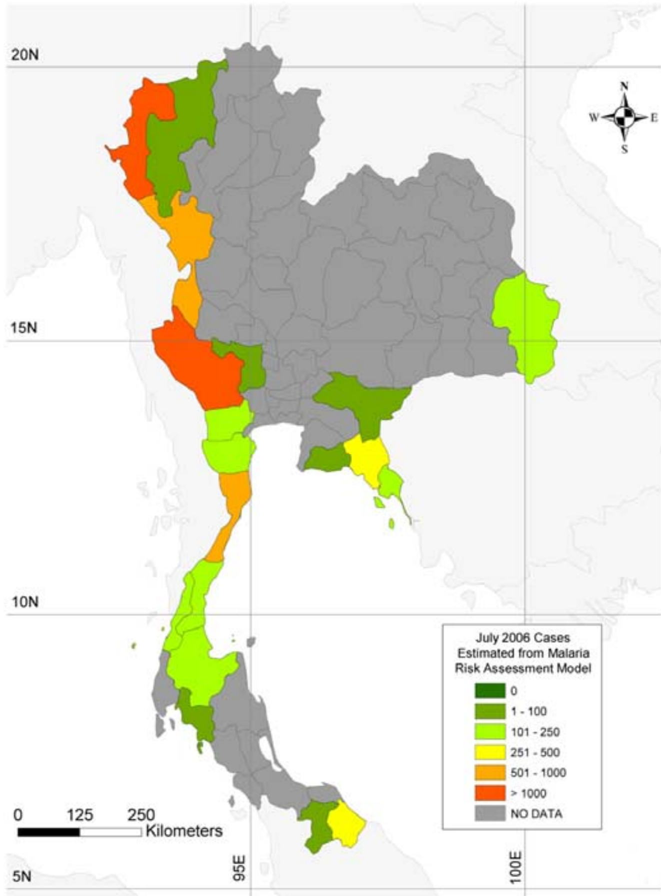

Figure 7. Current (July 2006) malaria cases estimated by the malaria risk assessment model for the 19 Thailand provinces more endemic with malaria.

5. DATA LIMITATIONS IN V&V

We have shown, through hindcasting, that the neural network model can reasonably well model the dependency on meteorological and environmental parameters and predict future cases. The development and V&V of the model, however, are limited by the availability of malaria data.

Because the malaria distribution is spatially heterogeneous, it would be desirable if malaria data of finer spatial resolution are available. But unfortunately, we have been able only to obtain very limited amount of district level data, which are insufficient for developing the malaria risk model. There is reason to believe, however, that higher resolution malaria data will correlate more closely with higher-resolution meteorological and environmental data and result in a risk model with higher accuracy.

To verify the accuracy of predicting malaria endemicity at the present or in the future, in general, it is necessary to compare model output with malaria cases of that timeframe. The malaria epidemiological data, however, is generally difficult to obtain. Thailand has stopped releasing the malaria data. Other developing countries, such as Indonesia, are limited by resources and public health capacity to properly collect and maintain malaria epidemiological data.

Our collaborators in the Armed Forces, such as AFRIMS and NAMRU2, do occasionally conduct active case detections or mass blood surveys when requested by the public health agencies in the host countries. These data, while undoubtedly have better quality than the average epidemiological data available in these countries, the sample size is usually small due to the limited scope of the surveys. The geographical distribution of the sampling points is also often limited. In addition, active case detection or mass blood survey are usually conducted at locations with ongoing or recent outbreaks. The slide positive rates at these locations are therefore higher than the endemicity in the general populations. Consequently the data may not be sufficiently representative for verifying the performance of the MMS risk assessment model.

If the official malaria epidemiological data are to become available again in Thailand, we would be able to properly test the prediction accuracy of the model. The model needs to be retrained, however, because socioeconomic factors and other contextual determinants might have changed appreciably in recent years.

6. CONCLUSIONS

Malaria transmission depends on the diverse factors that influence the vectors, parasites, human hosts, and the interactions among them. These factors may include, among others, meteorological and environmental condition, the innate and adapted immunity of the human hosts, public health system, housing standards, vector control, road construction, irrigation projects, and population movements. The couplings among these factors may be so complex that it is difficult to isolate the key factors that promote or sustain malaria transmission in an area.

The most apparent determinants are the meteorological and environmental factors, such as rainfall, temperature, humidity, and vegetation. For example, human experience has shown that malaria is correlated with the rainy season, and that ENSO events may either increase or decrease malaria transmission. When other factors remain more or less constant, the meteorological and environmental conditions can indeed be considered the driving factors. These conditions can be remotely sensed using satellites that regularly cover extensive geographical areas. Therefore, remote sensing has been used in recent years for developing malaria early warning systems, particularly for Africa. For the Greater Mekong Subregion, an epicenter of multi-drug resistant malaria, there have been few studies to examine the dependency of malaria cases on these factors.

We have shown that neural network techniques are a useful approach for modeling the dependency of malaria cases on meteorological and environmental parameters. Neural network is a vital part of machine or artificial intelligence, which is a discipline to study machine's ability for learning and adaptation, and exhibition of intelligent behaviors. In general, the neural network techniques are superior to generalized linear models, because linearization are subjective and may not be optimum.

Thailand has a long border—nearly 3,200 km over land—with Myanmar, Laos, Cambodia, and Malaysia as its neighboring countries. Significant populations from the neighboring countries have come into Thailand or stayed near the border over the last two decades. Along the Thai–Myanmar border, it is estimated by the World Health Organization (WHO) Border Health Program (WHO Thailand, 2005) that at the end of 2004, there were approximately 120,000 registered refugees living in camps, 400,000 registered migrant workers, and another 500,000 undocumented workers.

Taking the Tak Province for example, it is estimated that nearly a third of its population are refugees, migrants, or displaced populations. Because of the large border-crossing population movement, it may not be surprising that Tak is one of the most malaria endemic provinces in Thailand. Overall, approximately 70% of all malaria cases in Thailand occur in the 10 border provinces (WHO Thailand, 2005). Due to the limited accessibility of health care, the transient and migrant populations expand the human reservoir for malaria transmission. In turn, these populations escalate the endemicity among the native Thai population. The movement of migrant population is therefore an important contextual determinant that contributes to malaria transmission. In addition, it confounds the complexity for the prediction of malaria transmission intensity based on meteorological and environmental parameters.

We have used surface observed and satellite measured data to examine the dependency of malaria transmissions on meteorological and environmental factors. The malaria data are in provincial resolution, and the spatial resolution of the meteorological and environmental data are from medium to coarse. In spite of the coarse resolution of the malaria data, we have uncovered a reasonable degree of dependency on the meteorological and environmental parameters. Based on the dependency, we can assess the current and future malaria risks.

With the simplest neural network architecture, the average training accuracy is approximately 73% among the three leading malarious provinces. More complex architectures will result in a training accuracy approaching 84%. The average hindcasting accuracy is approximately 63% using the simplest (hence most robust) architecture. It should be noted that the training and testing accuracy are not meant to be 100%, because the meteorological and environmental parameters are only part of the factors that affect malaria transmissions.

Malaria transmission is known to be spatially heterogeneous. We have nevertheless extracted a reasonable amount of dependency on the meteorological and environmental parameters using malaria data at coarse resolution. There is reason to believe that we can obtain a more precise meteorological and environmental association by using malaria data at higher resolution. With the current results on hand, we will continue to seek to obtain malaria data at lower administrative levels (e.g., district or village). This would allow a more localized response to malaria warnings.

The risk assessments from the MMS project will allow the U.S. overseas forces to be better prepared for malaria prevention and in responding to malaria morbidity. In the Armed Forces, there are other Decision Support Systems similar to GSAT that provide risk assessments on infectious diseases. These systems exchange information with one another. To the best of our knowledge, at least two other decision support systems use malaria risk assessments information like what we will provide to GSAT. The beneficial returns of NASA data and results will be multiplied as the results from the MMS project are shared with other Decision Support Systems.

During peacetime or wartime, U.S. overseas forces work with the local public health organizations to reduce disease risks among the general populations. The outcome of the NASA MMS Project will therefore help reduce the morbidity and mortality among the local populations. The risk assessments will also facilitate more targeted insecticide and larvicide applications, and therefore reduce the potential damages to the environment and the risk of insecticide resistance.

ACRONYMS

AFRIMS	Armed Forces Research Institute for Medical Sciences
AFSOC	Air Force Special Operations Command
AVHRR	Advanced Very High Resolution Radiometer
CCD	Cold Cloud Duration
DAAC	Distributed Active Archive Center
DST	Decision Support Tool
ENSO	El Niño Southern Oscillation
EOS	Earth Observing System
GIS	Geographic Information System
GMS	Greater Mekong Subregion
GPM	Global Precipitation Measurement
GSAT	Global Situational Awareness Tool
MMS	Malaria Modeling and Surveillance
MODIS	Moderate Resolution Imaging Spectroradiometer
MOPH	Ministry of Public Health (Thailand)
NAMRU-2	Naval Medical Research Unit-2
NCAR	National Center for Atmospheric Research
NCEP	National Centers for Environmental Prediction
NDVI	Normalized Difference Vegetation Index
SIESIP	Seasonal-to-Interannual Earth Science Information Partner
TRMM	Tropical Rainfall Measuring Mission
V&V	Verification and Validation
WHO	World Health Organization

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